

(43) International Publication Date 15 January 2004 (15.01.2004)

PCT

## (10) International Publication Number WO 2004/005321 A3

(51) International Patent Classification<sup>7</sup>: A61K 31/44, 31/445, C07D 211/72

A01N 43/40,

(21) International Application Number:

PCT/US2003/021178

(22) International Filing Date:

2 July 2003 (02.07.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/394,339

3 July 2002 (03.07.2002) US

(71) Applicant (for all designated States except US): THE ROCKEFELLER UNIVERSITY [US/US]; 1230 York Avenue, New York, NY 10021-6399 (US).

(71) Applicant and

(72) Inventor: HANAUSKE-ABEL, Hartmut, M. [DE/US]; 1055 River Road, Apt. 510 South, Edge Water, NJ 07020 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): POPOWICZ, Anthony [US/US]; 53 Crestwood Lane, Farmingville, NY 11738 (US).

(74) Agents: GOLDMAN, Michael, L. et al.; Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY 14603-1051 (US). (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## **Published:**

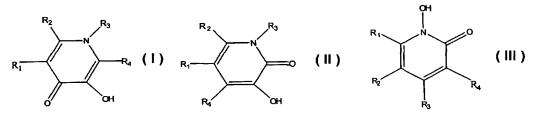
with international search report

 before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 15 April 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF INHIBITING 4-HYDROXYPHENYLPYRUVATE DIOXYGENASE IN A LIVING SYSTEM



(57) Abstract: The present invention is directed to a method of inhibiting 4-hydroxyphenylpyruvate dioxygenase in a living system by administering to the living system an effective amount of a compound of formulas I or II or III or derivatives thereof as follows: R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> each individually represent a hydrogen, an alkyl, alkenyl, or alkoxy group containing 1 to about 8 carbon atoms, an aryl, aralkyl, or cycloalkyl group containing about 5 to 12 carbon atoms, or a carboalkoxy or carbamyl group containing up to 8 carbon atoms, or a peptide or peptidomimetic moiety containing 10 to about 30 carbon atoms under conditions effective to inhibit 4- hydroxyphenylpyruvate dioxygenase in the living system. These compounds are also useful in carrying out a method of treating a patient and a method of regulating plant growth.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/21178

A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : A01N 43/40; A61K 31/44, 31/445; C07D 211/72  US CL : 504/255: 514/330, 348: 546/296						
US CL: 504/255; 514/330, 348; 546/296 According to International Patent Classification (IPC) or to both national classification and IPC						
B. FIELDS SEARCHED						
Minimum documentation searched (classification system followed by classification symbols) U.S.: 504/255; 514/330, 348; 546/296						
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched						
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet						
C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category *	Citation of document, with indication, where a	ppropriate, o	f the relevant passages	Relevant to claim No.		
X	X WALDMEIER et al. Inhibition of Catechol-O-Methyltransferase (COMT) as well as			1, 2		
Tyrosine and Tryprophan Hydroxylase by the Orally Active Iron Chelator, 1,2-Dimethyl-3 Hydroxypyridin-4-one (L1, CP20), in Rat Brain In Vivo, Biochemical Pharmacology, March 1993, Vol 45. No. 12, pages 2417-2424.			mical Pharmacology,	3-6		
A	US 6,118,050 A (STURNER et al) 12 September 2000 (12.09.2000), columns 1-2.			5, 6		
				·		
	documents are listed in the continuation of Box C.		ee patent family annex.			
•	pecial categories of cited documents:	d	ater document published after the inter late and not in conflict with the applica	ation but cited to understand the		
"A" document of particul	defining the general state of the art which is not considered to be ar relevance	P	principle or theory underlying the inve	ntion		
"E" earlier app	olication or patent published on or after the international filing date	c	locument of particular relevance; the considered novel or cannot be consider when the document is taken alone	claimed invention cannot be ed to involve an inventive step		
"L" document establish ti specified)	which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"Y" d	locument of particular relevance; the considered to involve an inventive step combined with one or more other such	when the document is		
"O" document	referring to an oral disclosure, use, exhibition or other means		being obvious to a person skilled in the			
	published prior to the international filing date but later than the te claimed	"&" document member of the same patent family				
Date of the ac	tual completion of the international search	Date of mailing of the international search report				
02 October 2003 (02.10.2003)						
Name and mailing address of the ISA/US  Mail Stop PCT, Attn: ISA/US  Commissioner for Patents P.O. Box 1450		Authorized officer  Authorized Dell-Harris for Marina Lamm				
Alex	andria, Virginia 22313-1450 (703)305-3230	Telephone No. (703) 308-1235				

	PCT/US03/21178	<del></del>
INTERNATIONAL SEARCH REPORT	PC1/0303/211/6	•
1 21224 WITO WILL SPANON REI ON I		
	<u> </u>	
		•
		•
Continuation of D. EIEI DO CHARGING IV.		
Continuation of B. FIELDS SEARCHED Item 3:		
WEST, STN (file medicine) search terms: tyrosinemia, hypertyrosinemia, tyrosine, deferiprone, dmhp, 4hppd,	nymivate plant herbicide	
Jermin, Types, Jermin, and Jer	pyravate, plant, herofette	

Form PCT/ISA/210 (second sheet) (July 1998)